Remarks/Arguments

In a Final Office Action mailed March 23, 2006, the Examiner in charge of the above-identified application maintained the provisional obviousness-type double patenting and 35 U.S.C. § 103(a) rejections. In light of the arguments below, applicants respectfully request reconsideration.

Claim Rejections – 35 U.S.C. § 103

Claims 5-7 and 9-11 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Alfenito (U.S. Patent No. 6,355,419) in view of applicant's alleged admission of the prior art and Butler (U.S. Patent No. 6,589,726). This rejection is respectfully traversed.

At the outset, applicants wish to clarify for the record that no admission of prior art was made with respect to the claimed embodiments in the prosecution of the present application. Applicants agree the specification provides at page 3, [00014] that "...the [claimed] method utilizes a well-established hydrophobic property of the trityl moiety." However, as articulated in applicants response mailed December 28, 2005, the trityl chemistry behind the fabrication of the hydrophobic barrier is not the basis for the invention. There appears to be a misunderstanding between the basis for using trityl protected phosphoramidite in preparing the microarrays and the main inventive concept underlying the claimed embodiments.

The basis for the present invention is using a common array synthesizing instrument to fabricate both oligonucleotide probes and the hydrophobic barrier without any prior treatment of the substrate. The trityl group is simply a preferred moiety that provides the desired hydrophobic property for preparing the hydrophobic barrier surrounding each subarray on the microarray. The trityl moiety is not the main inventive concept of the claimed embodiment, rather it is a tool to carry out the concept. Thus, by stating the hydrophobic property of the trityl moiety is well-established, applicants made no "prior art" admissions involving the claimed embodiments.

Next, as to the cited documents, applicants re-submit that Alfenito alone or combined with Butler fails to disclose or suggest the inventive concept of using a common microarray synthesis instrument to fabricate both (1) the oligonucleotide probes and (2) the hydrophobic barrier surrounding each subarray on the microarray. Alfenito discloses making a microarray

by depositing probes on a substrate and then applying a separate material or process to make hydrophobic areas between features of the array. Alfenito discloses the use of a hydrophobic grid membrane filter (HGMF), such as the ISO-GRID™ from QA Laboratories, Ltd., as a hydrophobic barrier. This filter is a purchased item imposed on the array rather than a barrier fabricated by a microarray synthesis instrument on the array (see Alfenito at column 23, lines 13-27.) Alfenito also teaches the use of a solution of silicone in an appropriate solvent as a hydrophobic barrier (see Alfenito at column 64, lines 4-9.)

By contrast, the method of the present application uses a common instrument to prepare both the array-immobilized probe sets and the hydrophobic areas. There are clear differences in process between the applicants' method and that of Alfenito. The applicants assert this difference in process is clearly reflected in the claims and is a non-obvious difference because nothing in Alfenito suggests using the same instrument to construct both the probes and hydrophobic areas on the array. This is unprecedented in the art and it was not obvious before the work described in the present specification that this could be accomplished.

Moreover, it is noteworthy that in making a microarray on a scale in which many features are constructed, the features are quite small. The specification discusses that up to 786,432 features can be constructed on an area of a microscope slide in a micromirror based instrument. To effectively perform the claimed method, precision in the fabrication of the elements of the microarray is required. See a discussion on this topic in the specification paragraphs 15 to 17. In order to construct the features in the array and the hydrophobic areas between features with precision, it is enormously helpful for the same instrument to be used for both parts of the process, so the two fabrications can be performed without moving the substrate and therefore without losing alignment.

The present invention enables and facilitates such precision, Alfenito does not. This method enables the fabrication of very small and dense features with hydrophobic barriers between them, in a way that Alfenito does not. Nothing in Alfenito discusses using the same instrument to make both the probes and the hydrophobic regions. Nowhere in Alfenito does it discuss keeping the substrate fixed in position while both processes are performed. Also, nothing in Alfenito provides a motivation for anyone to perform the processes as the applicants do here. Accordingly, Alfenito cannot make obvious the claimed methods.

Next, it is submitted that since applicants have shown the primary document relied on by the Examiner, Alfenito, fails to teach or suggest the claimed subject matter, the secondary document, Butler, must also fail. Butler does not disclose the missing features and does not cure the deficiencies of Alfenito. Butler discloses methods for fabricating solid supports (i.e., arrays) for *in situ* polynucleotide synthesis. Butler's array fabrication methods use photoresist substances, such as, an optical positive *photoresist substance* or an E-beam positive photoresist substance, *to coat the support surface (substrate)* and to act as a physical barrier separating the hydrophilic and hydrophobic derivatization processes. (see Butler at col. 10, line 14; col. 14, line 37; and Claims 1 and 2.)

By contrast, applicants affirmatively recite in the specification that the hydrophobic barrier is constructed using a MAS™ instrument without prior special treatment of the substrate. A digital micromirror device (DMD) is used to direct light to the location of the hydrophobic barrier. This characteristic allows the hydrophobic barrier to be constructed in place by the MAS™ instrument itself without prior treatment of the substrate. (see present specification at pgs. 3-4, paragraphs 13-15.) This approach facilitates efficient fabrication of array probe sets and hydrophobic areas surrounding the subarrays to be performed with great precision, without moving the substrate or losing alignment.

Furthermore, applicants discern no reasonable basis or motivation for attempting to combine or modify the method of Alfenito by Butler to practice the claimed embodiments. Based on these patentable differences, it would not be obvious to one of the ordinary skill in the art to modify the method and product of Alfenito as per the microarray fabrication method of Butler to develop the method described in the application. Thus, Alfenito in view of Butler do not render obvious the claimed methods.

Double Patenting

The Examiner maintained the provisional obviousness-type double patenting rejection drawn to Claims 5-7 and 9-11 as being unpatentable over claims of copending Application No. 10/674,768.

Applicants acknowledge the provisional rejection and the suggestion of filing a terminal disclaimer. However, applicants submit that based on the arguments in our prior

response and herein below, it is believed that a provisional double patenting rejection is unwarranted. Thus, this rejection is also traversed.

The disclosure of Application No. 10/674,768 does mention the concept of hydrophobic barriers, but the claims of the '768 application and the claims of the present application are quite distinct and not overlapping. In fact, the claims of the '768 application are directed to methods for loading samples onto an array while the methods of the present invention are directed at methods for fabricating arrays with hydrophobic barriers. Thus, the two technologies are distinct and not obvious one in view of the other.

One ordinary skill in the art can readily gleam by a cursory review of the independent claims that the objectives and the manner in which those objectives are carried out are different between the two applications. There are limitations in the claims of each case which are not in the claims of the other and the Examiner has not demonstrated why those differences are obvious. For example, the independent claims of the '768 application do not disclose hydrophobic barriers surrounding the subarray of the microarray and the presence of hydrophobic barriers is not encompassed in the independent claims. Hydrophobic barriers are listed merely as optional in the '768 application.

Also, the presently claimed embodiments are not inherently produced by the methods of the '768 application and *vice versa*. There is no requirement the hydrophobic barriers surrounding the subarrays of the microarray be present for a skilled person to effectively practice the method of the '768 application. Thus, it is believed that this rejection is misplaced and should be withdrawn after reconsideration.

Furthermore, applicants note that co-pending application '768 has not yet issued as a patent and a terminal disclaimer is still premature at this stage.

In view of these remarks, Applicants respectfully requests prompt and favorable consideration of this response and that a timely Notice of Allowance be issued in this case.

A petition for extension of time and a Request for Continuing Examination (RCE) are enclosed herewith so this response will be considered as timely filed. Please charge these fees to Deposit Account No. 17-0055. If any other fee is due regarding this response or any

other response, please consider this a request to charge the fee to Deposit Account No. 17-0055.

Respectfully submitted,

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